PATENT
Attorney Docket No.: A-68851-1/RMS/DCF/SRN

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:	
LEBL et al.	Patent Examiner: W. Beisner
Serial No.: 09/493,741	Group Art Unit: 1744
Filed: January 28, 2000	
For: *Apparatus and Method for Separation of Liquid Phases of Different Densities and for Flourous Phase Organic Syntheses*	

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CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8 - FIRST CLASS MAIL

I hereby certify that this correspondence, including listed enclosures, is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Box Fee Amendment, Washington, DC 20231 on DECEMBER 5, 2001

Signed: _____
Maria Ciganovich

AMENDMENTS AND RESPONSE TO OFFICE ACTION

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

This amendment is in response to the Official Action dated June 5, 2001 received in the above-identified application. A petition for a three (3) month extension of time with the appropriate fee is enclosed, making this a timely response. The Commissioner is authorized to charge any additional fees, including any extension fees, which may be required, or credit any overpayment to Deposit Account No. 06-1300 (Our Order No. A-68851-1/RMS/DCF/SRN).

The Applicants request that the following amendments be made and that the remarks set forth thereafter be considered.

AMENDMENTS

Please amend the above-identified application as follows:

In the Claims:

Please cancel claims 1-26 without prejudice or disclaimer as drawn to non-elected inventions.

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A1

27. (Amended) An apparatus comprising:

a) a centrifuge comprising a rotor designed to hold reaction vessels at a tilt away from the axis of rotation; and

b) a waste reservoir connected to said centrifuge to hold liquids expelled from said reaction vessels.

In the Background of the Invention:

Please make all references to U.S. Patent Application Serial No. 08/815,975 read U.S. Patent 6,045,755 on page 2 lines 7, 10, and 11.

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(Amended) The productivity of automated instruments can be dramatically improved by use of disposable reaction vessels (such as multititer plates or test tube arrays) into which reagents are added by pipetting, or by direct delivery from storage containers. The optimal storage vehicle is a syringe-like apparatus of a material inert to the chemical reactants, etc., e.g., a glass syringe, allowing the storage of the solution without any exposure to the atmosphere, and capable of serving as a delivery mechanism at the same time. See U.S. Patent 6,045,755. An alternative technique based on the removal of upper layer of liquid by suction from the surface above the separated layers is limited to the arrays of up to a hundred of suctions (For similar situation in solid phase synthesis see U.S. Patent 6,045,755. The present application is

an improvement upon U.S. Patent nos 5,202,418, 5,338,831, 5,342,585, and 6,045,755 which describe placement of resin in polypropylene mesh packets and removal of liquid through the openings of these packets, or removal of the liquid from the pieces of porous textile-like material by centrifugation, or removal of liquid phase from the solid phase by centrifugation of tilted plates. Liquid removal by centrifugation was described and is the subject of several publications (*see* the book "Aspects of the Merrified Peptide Syntheses" by Christian Birr in the series Reactivity and Structure Concepts in Organic Chemistry vol. 8, K. Hafner, J.-M. Lehn, C.W. Rees, P. von Rague, Schleyer, B.M. Trost, R. Zahradnik, Eds., Sringer-Verlag, Berlin, Heidelberg, New York, 1978, and German Patent Application P 20 17351.7, G. 70 13256.8, 1970. these references describe the use of centrifugation for liquid removal from slurry of solid phase particles in a concentrical vessel equipped with a filtration material in its perimeter and spun around its axis. See also WO99/25470, hereby expressly incorporated by reference in its entirety.

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In the Detailed Description of the Invention:

At page 11, line ~~18~~ 8, please replace the paragraph with the following rewritten paragraph:

(Amended) The stepwise solid phase synthesis of peptides is well known. An exemplary solid-phase combinatorial protocol is that for the synthesis of peptides attached to polymer resin, which proceeds according to Lam et al., 1991, Nature 354:82-84; U.S. Patent 5,510,240; Lam et al., 1994, Selective technology: Bead-binding screening. Methods: A Companion to Methods in Enzymology 6:372-380. Another exemplary protocol is that for the synthesis of benzodiazepine moieties, which proceeds according to Bunin et al., 1992, J. Amer. Chem. Soc., 114:10997-10998 and U.S. Patent 5,288,514. Also, for protocols for the addition of N-substituted glycines to form peptides, see, e.g., Simon, et al., 1992, Proc. Natl. Acad. Sci. USA, 89:9367-9371; Zuckermann et al., 1992, J. Amer. Chem. Soc., 114:10646-10647; WO

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PCT94/06,451 to Moos et al.; Approaches for synthesis of small molecular libraries were recently reviewed by, e.g., Krchnak and Lebl, 1996, Molecular Diversity, 1:193-216; Ellman, 1996, Account. Chem. Res., 29:132-143; Armstrong et al., 1996, Account. Chem. Res., 29:123-131.; Fruchtel et al., 1996, Angew. Chem. Int. Ed., 35:17-42; Thompson et al., 1996, Chem. Rev., 96:555-600; Rinnova et al., 1996, Collect. Czech. Chem. Commun., 61: 171-231; Hermkens et al., 1996, Tetrahedron, 52:4527-4554. Exemplary building blocks and reagents are amino acids, nucleosides, other organic acids, aldehydes, alcohols, and so forth, as well as bifunctional compounds, such as those given in Krchnak and Lebl, 1996, Molecular Diversity, 1:193-216.

A 3

At page 12, lines 21 and 36, please replace the paragraphs with the following rewritten paragraphs:

(Amended) The nucleic acids may contain any combination of deoxyribo- and ribo-nucleotides, and any combination of bases, both naturally occurring and synthetic, including uracil, adenine, thymine, cytosine, guanine, inosine, xanthine, hypoxanthine, isocytosine, isoguanine, etc. A preferred embodiment utilizes isocytosine and isoguanine in nucleic acids designed to be complementary to other probes, rather than target sequences, as this reduces non-specific hybridization, as is generally described in U.S. Patent No. 5,681,702. As used herein, the term "nucleoside" includes nucleotides as well as nucleoside and nucleotide analogs, and modified nucleosides such as amino modified nucleosides or phosphoramidite nucleosides. In addition, "nucleoside" includes non-naturally occurring analog structures. Thus for example the individual units of a peptide nucleic acid, each containing a base, are referred to herein as a nucleoside.

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(Amended) The stepwise synthesis of nucleic acids is well known, and generally involves the stepwise addition of protected, activated nucleoside monomers to a solid support, followed